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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,389	10/07/2003	John H. Kenten	IGN-2005US02	7446

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EXAMINER	
POPA, ILEANA	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/681,389	KENTEN ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *80 and 94-101* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *80 and 94-101* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/04/2008 has been entered.

Claims 1-79 and 81-93 have been cancelled. Claims 80 and 94 have been amended.

Claims 80 and 94-101 are pending and under examination.

2. The following rejections are withdrawn in response to Applicant's amendment to the claims filed on 09/04/2008:

The rejection of claims 89 and 94-101 under 35 U.S.C. 112, first paragraph, as introducing new matter;

The rejection of claims 80 and 101 under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. (J Immunol, 1996, 1545: 4796-4804), in view of both Kierrulf et al. (Mol Immunol, June, 1997, 34: 599-608, Abstract) and Tang et al. (Nature, 1992, 356: 152-154);

The rejection of claims 80, 94-97, 100, and 101 under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. taken with Kierrulf et al. and Tang et al., in further view

of each Ferro et al. (Eur J Cancer, 1997, 33: 1468-1478, of record), Sacca (Cardiovascular Research, 1997, 36: 3-9, of record), and Johnston et al. (U.S. Patent No. 5,703,057);

The rejection of claims 80, 98, and 101 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Dalum et al. taken with Kierrulf et al. and Tang et al., in further view Hohlfeld (Multiple Sclerosis, 1996, 1: 376-378).

New Rejections

Claim Rejections - 35 USC § 112, 2nd paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 80 and 94-101 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 80 and 94 are drawn to a method of inducing an immune response/reducing the level of a predetermined protein by administering a DNA encoding a fusion protein, wherein "one or more epitopes are recognized by an antibody to be detected". There is no nexus between inducing an immune response/reducing protein levels and "an antibody to be detected", which antibody is recited before the step of introducing the DNA construct into an animal. As such, there is nothing in the claims which would clearly indicate that the "antibody" is the result of introducing the construct into the animal. The recitation of "an antibody to be detected" is vague

because, by reading the claims, one of skill in the art would not know how such a recitation relates to the method or how such an antibody defines the structure of the claimed fusion protein.

Claims 95-101 are rejected for being dependent from the rejected claim 94 and also for failing to further clarify the basis of the rejection.

Claim Rejections - 35 USC § 112, 1st paragraph - enablement

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 80 and 94-101are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of stimulating an immune response/reducing the level of a predetermined protein in an animal by administering a DNA construct encoding tandem heat shock protein fusion comprising an epitope-containing segment, wherein the DNA construct is operably linked to a promoter, does not reasonably provide enablement for a method of stimulating an immune response/reducing the level of a predetermined protein in an animal by providing a DNA construct encoding a tandem heat shock protein fusion comprising an epitope-containing segment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC § 112, first

paragraph, have been described by the court in *In re Wands,* 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skills of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided.

The instant claims recite methods of inducing an immune response or reducing the levels of a predetermined protein in an animal by administering to an animal a DNA construct encoding a fusion protein. The recitation of a DNA construct encoding a fusion protein does not require a DNA operably linked to a promoter; such a broad recitation encompasses any DNA construct as long as it encodes a fusion protein, including DNAs encoding the fusion protein wherein the DNAs are not operably linked to a promoter. Inducing an immune response requires the expression of the encoded fusion protein; one of skill in the art would readily realize that DNA constructs could not be expressed if they are not operably linked to promoters. As such, one of skill the art would know that, unless the DNAs constructs are operably linked to promoters, the mere administration of DNA constructs would not be able to induce an immune response. Neither the art nor the specification provides any example or guidance as to

how to perform the claimed method by using a DNA construct which is not operably linked to a promoter, as encompassed by the instant claims. Therefore, one of skill in the art would not recognize that the claimed invention is enabled to its entire claimed scope.

Amending the claims to specify that the DNA construct is operably linked to a promoter would obviate this rejection.

7. Claims 94-100 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of reducing the levels of a predetermined protein by administering a DNA construct encoding tandem heat shock protein fusion comprising an epitope-containing segment, wherein the DNA construct is operably linked to a promoter and wherein the epitopes-containing segment is derived from the predetermined protein, does not reasonably provide enablement for a method of reducing the levels of a predetermined protein by administering a DNA construct encoding tandem heat shock protein fusion comprising an epitope-containing segment. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

It is noted that both the art and the specification teach that reducing the levels of a predetermined protein requires inducing antibodies against the predetermined protein. However, the claims recite a fusion protein comprising “an epitope-containing segment”. Such a broad recitation encompasses any epitope-containing segment derived from any

protein other than the predetermined protein. One of skill in the art would not recognize that the administration of any epitope-containing segment derived from any protein, as broadly claimed, would induce an antibody response against the predetermined protein, wherein the antibody response results in reducing the level of the predetermined protein. Therefore, one of skill in the art would not recognize that the claimed invention is enabled to its entire claimed scope.

Amending the claims to specify that the epitope-containing segment is derived from the predetermined protein would obviate this rejection.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 80, 94, and 101 are rejected under 35 U.S.C. 102(e)/or 102(a) as being anticipated by Mizzen et al. (U.S. Patent No. 7,157,089).

Mizzen et al. teach a method of stimulating the immune response against a fusion protein in an animal, the method comprising administering to the animal vaccine comprising an expression vector encoding a fusion protein comprising two contiguous

heat shock proteins fused to a protein (i.e., a predetermined protein and an epitope containing segment); the heat shock proteins could be ubiquitin (claims 80 and 101) (column 4, lines 55-67; column 7, lines 1-9; column 11, line 66 to column 12, line 3; column 13, line 67 to column 14, line 2; column 15, lines 29-34). Mizzen et al. also teach their vaccine as being suitable to induce a humoral immune response against predetermined proteins (i.e., antibodies recognizing protein epitopes) (column 14, lines 45-51). With respect to the method of reducing the level of a predetermined protein (claim 64), it is noted that all claim 64 requires is the administration of a nucleic acid encoding a fusion protein comprising ubiquitin and an epitope-containing segment. Therefore, by teaching administering their nucleic acid encoding a fusion protein between ubiquitin and a predetermined protein to induce an immune response against the predetermined protein, Mizzen et al. also anticipate claim 94. Since Mizzen et al. teach all claim limitations, the claimed invention is anticipated by the above-cited art.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 80, 94-97, and 99-101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizzen et al., in view of each Ferro et al. (Eur J Cancer, 1997, 33: 1468-1478, of record), Tang et al. (Nature, 1992, 356: 152-154, of record), Sacca

(Cardiovascular Research, 1997, 36: 3-9, of record), and Johnston et al. (U.S. Patent No. 5,703,057, of record).

The teachings of Mizzen et al. are applied as above for claims 80, 94, and 101.

Mizzen et al. do not teach the predetermined protein as being gonadotropin releasing hormone (GnRH) (claims 95-97) or a growth hormone (claim 99). Ferro et al. teach reducing the levels of GnRH for immunocastration and anti-tumor treatment (claims 95-97) (Abstract, p. 1475, column 1, p. 1477, column 2). With respect to the limitation of growth hormone (claim 99), Tang et al. teach DNA vaccines as being able to produce an efficient immune response against the human growth hormone (hGH) (Abstract, p. 152, column 2 bridging p. 153). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Mizzen et al. by using a DNA vaccine encoding a fusion ubiquitin-GnRH or ubiquitin-hGH, with a reasonable expectation of success. The motivation to use an anti-GnRH vaccine is provided by Ferro et al. who teach the utility of immunoneutralizing GnRH for lowering the estradiol levels and therefore as a potential therapy in estrogen-sensitive disorders such as polycystic ovary syndrome and hormone-dependent breast cancer (p. 1468, column 1 bridging column 2). Additionally, one of skill in the art would have been motivated to immunoneutralize hGH because the art prior teaches that an excess of hGH is associated with certain diseases, such as acromegaly (see Sacca, p. 4, column 1 and 2). One of skill in the art would have been expected to have a reasonable expectation of success because the art teaches the successful use of DNA constructs encoding ubiquitin fusion proteins to elicit antibody responses in animals. With respect

to the limitation of the fusion protein being conjugated to a non-ubiquitin carrier protein (claim 100) such was routine in the art at the time the invention was made. For example, Johnston et al. teach conjugation of ubiquitin fusion proteins with non-ubiquitin carrier proteins, such as KLH or BSA, to increase the immunogenicity of ubiquitin fusion proteins (column 24, lines 44-55). Therefore, one of skill in the art would have known and would have been motivated to further modify the ubiquitin fusion proteins according to the teachings of Johnston et al. to increase their immunogenicity. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

12. Claims 80, 94, 98, and 101 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizzen et al., in view Hohlfeld (Multiple Sclerosis, 1996, 1: 376-378, of record).

The teachings of Mizzen et al. are applied as above for claims 80, 94, and 101. Mizzen et al. do not teach neutralizing the biological function of tumor necrosis factor (TNF) (claim 98). Hohlfeld teaches the use of antibodies to inhibit TNF-α activity as a treatment for multiple sclerosis (Abstract, p. 377, column 1 bridging column 2). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Mizzen et al. by using a DNA vaccine encoding a fusion ubiquitin-TNF-α, with a reasonable expectation of success. The motivation to use an anti- TNF-α vaccine is provided by Hohlfeld who teaches the utility of immunoneutralizing TNF-α activity for the treatment of diseases such as multiple sclerosis and rheumatoid arthritis (p. 377, column 1 bridging column 2). One of skill in the art would have been expected

to have a reasonable expectation of success because the art teaches the successful use of DNA constructs encoding ubiquitin fusion proteins to elicit antibody responses in animals. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

13. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
Examiner, Art Unit 1633